

WHAT IS CLAIMED IS:

1. A teleost embryo comprising a polynucleotide analogue, wherein said embryo is of a teleost species that undergoes meroblastic cleavage, and wherein said analogue is present in an amount effective to reduce expression from a selected nucleic acid in said embryo.
2. The embryo of claim 1, wherein said embryo is selected from the group consisting of a zebrafish embryo, a puffer fish embryo, a medaka embryo, and a stickleback embryo.
3. The embryo of claim 2, wherein said embryo is a zebrafish embryo.
4. The embryo of claim 1, wherein said selected nucleic acid is an mRNA.
5. The embryo of claim 4, wherein said analogue is complementary to a region of said mRNA that comprises the 5' untranslated region of said mRNA.
6. The embryo of claim 4, wherein said analogue is complementary to a region of said mRNA that comprises part of or the entire AUG start codon of said mRNA.
7. The embryo of claim 4, wherein said analogue is complementary to a region of said mRNA that comprises the coding region of said mRNA.
8. The embryo of claim 1, wherein said analogue is 9 to 90 bases in length.
9. The embryo of claim 1, wherein said analogue is 15 to 50 bases in length.
10. The embryo of claim 1, wherein said analogue is 20 to 30 bases in length.
11. The embryo of claim 1, wherein said analogue is a morpholino-modified polynucleotide.
12. The embryo of claim 1, wherein said analogue is a 3'-5' phosphoroamidate.
13. The embryo of claim 1, wherein said analogue is a peptide nucleic acid.
14. The embryo of claim 1, wherein said analogue is a polynucleotide containing a ribose moiety that has a 2' O-methyl group.
15. The embryo of claim 1, wherein at least 15 % of the nucleotides in said analogue are not complementary to the corresponding nucleotides in said selected nucleic acid.
16. The embryo of claim 1, wherein said analogue is complementary to a nucleic acid of said embryo, said nucleic acid having a coding sequence that has a homologue or orthologue in another species.

17. The embryo of claim 1, wherein reduction in expression from said nucleic acid persists to larval or post-hatching stages of development.
18. The embryo of claim 1, wherein said embryo further comprises an exogenous rescue mRNA that encodes a polypeptide whose expression is reduced by said polynucleotide analogue, wherein said rescue mRNA is present in an amount sufficient for expression of said polypeptide at a level comparable to that in embryos free of said analogue.
19. The embryo of claim 1, further comprising at least one additional polynucleotide analogue, wherein said embryo is of a teleost species that undergoes meroblastic cleavage, wherein said polynucleotide analogues are complementary to different regions of said selected nucleic acid, and wherein said analogues are present in amounts effective to reduce expression from said selected nucleic acid.
20. The embryo of claim 1, further comprising at least one additional polynucleotide analogue, wherein said embryo is of a teleost species that undergoes meroblastic cleavage, wherein said polynucleotide analogues are complementary to different nucleic acids, and wherein said analogues are present in amounts effective to reduce expression from said different nucleic acids.
21. A method for producing a teleost embryo comprising a polynucleotide analogue, wherein said teleost embryo is of a species that undergoes meroblastic cleavage, and wherein said analogue is present in an amount effective to reduce expression from a selected nucleic acid in said embryo, said method comprising contacting said embryo, or an egg giving rise to said embryo, with said polynucleotide analogue.
22. The method of claim 21, wherein said step of contacting comprises injecting said analogue into said embryo or egg giving rise to said embryo, or adding said analogue to the surface of said embryo or egg giving rise to said embryo.
23. The method of claim 21, wherein said embryo or egg giving rise to said embryo is selected from the group consisting of a zebrafish embryo or egg giving rise to said zebrafish embryo, a puffer fish embryo or egg giving rise to said puffer fish embryo, a medaka embryo or egg giving rise to said medaka embryo, and a stickleback embryo or egg giving rise to said stickleback embryo.

24. A composition comprising a morpholino-modified polynucleotide and a buffer having a pH similar to the pH within a teleost egg or embryo, wherein said morpholino-modified polynucleotide is complementary to a selected nucleic acid.
25. The composition of claim 24, wherein said buffer is isotonic to said teleost egg or embryo.
26. The composition of claim 24, wherein said buffer is Danieau buffer.
27. The composition of claim 24, wherein said teleost egg or embryo is of a species that undergoes meroblastic cleavage.
28. The composition of claim 24, wherein said teleost egg or embryo is selected from the group consisting of a zebrafish egg or embryo, a puffer fish egg or embryo, a medaka egg or embryo, and a stickleback egg or embryo.
29. The composition of claim 24, wherein said teleost egg or embryo is a zebrafish egg or embryo.
30. The composition of claim 24, further comprising a rescue mRNA, wherein said rescue mRNA encodes a polypeptide whose expression is reduced by said morpholino-modified analogue.
31. The composition of claim 24, further comprising at least one additional polynucleotide analogue, wherein said polynucleotide analogues are complementary to different regions of said selected nucleic acid.
32. A method for determining a phenotype associated with a selected nucleic acid in a teleost embryo or egg giving rise to said embryo, wherein said embryo or egg is of a teleost species that undergoes meroblastic cleavage, said method comprising:
 - (a) contacting said teleost embryo or egg giving rise to said embryo with a morpholino-modified polynucleotide analogue that targets said selected nucleic acid; and
 - (b) detecting an altered phenotype in said teleost embryo or egg, or embryo developing from said egg, wherein said altered phenotype is associated with reduced expression or altered function of said selected nucleic acid.
33. The method of claim 32, wherein said selected nucleic acid is a maternal or zygotic nucleic acid.
34. The method of claim 32, wherein said altered phenotype is observed from

fertilization, through organogenesis, to the completion of embryogenesis.

35. The method of claim 32, said method further comprising contacting said embryo or egg giving rise to said embryo with a rescue mRNA, wherein said rescue mRNA encodes a polypeptide whose expression is reduced by said analogue, and wherein said rescue mRNA is present in an amount sufficient for expression of said polypeptide at a level comparable to that of a teleost embryo, or egg giving rise to said embryo, that is free of said analogue.
36. A method for determining if a phenotype mediated by a polynucleotide analogue in a teleost organism is sequence-specific, said method comprising:
- a) contacting a first teleost embryo or teleost egg with said polynucleotide analogue;
 - b) assessing the phenotype of said first teleost embryo or egg, or a teleost embryo developing from said egg, subsequent to step (a);
 - c) contacting a second teleost embryo or teleost egg with (i) said polynucleotide analogue and (ii) a rescue mRNA molecule;
 - d) assessing the phenotype of said second teleost embryo or egg, or a teleost embryo developing from said egg, subsequent to step (c); and
 - e) comparing the results of (b) and (d), wherein a phenotype detected in (b) that is not detected in (d) indicates that said phenotype detected in (b) is sequence-specific.
37. A method of determining if first and second polypeptides are genetic interactors, said method comprising:
- a) contacting a first teleost embryo or teleost egg with a first polynucleotide analogue that targets a nucleic acid encoding said first polypeptide, and assessing the phenotype of said teleost embryo or egg, or a teleost embryo developing from said egg;
 - b) contacting a second teleost embryo or egg giving rise to said embryo with a second polynucleotide analogue that targets a nucleic acid encoding said second polypeptide, and assessing the phenotype of said teleost embryo or egg, or a teleost embryo developing from said egg;
 - c) contacting a third teleost embryo or egg giving rise to said embryo with

said first and second polynucleotide analogues, and assessing the phenotype of said teleost embryo or egg, or a teleost embryo developing from said egg; and

- d) comparing the results of (a), (b), and (c), wherein said two polypeptides are genetic interactors if the phenotype observed in (c) is different from the sum of the individual phenotypes observed in (a) and (b).

- 38. The method of claim 37, wherein said phenotype observed in (c) is more or less extensive than said sum of the individual phenotypes observed in (a) and (b).
- 39. A kit comprising a collection of different morpholino-modified polynucleotides, wherein said different morpholino-modified polynucleotides are effective to reduce expression from different nucleic acids, and wherein said different nucleic acids are involved in a common metabolic process.
- 40. A collection of morphants, wherein each morphant is generated by a different morpholino-modified polynucleotide selected from a collection of morpholino-modified polynucleotides effective to reduce expression from different nucleic acids, and wherein said different nucleic acids are involved in a common metabolic process.
- 41. A teleost morphant defective in development of a differentiated tissue.
- 42. The morphant of claim 41, wherein said differentiated tissue is pancreas.
- 43. The morphant of claim 41, wherein said differentiated tissue is vasculature tissue.
- 44. The morphant of claim 41, wherein said differentiated tissue is blood.
- 45. The morphant of claim 41, wherein said differentiated tissue is an eye.
- 46. The morphant of claim 41, wherein said differentiated tissue is the central neural system.
- 47. The morphant of claim 41, wherein said differentiated tissue is a muscle.
- 48. The morphant of claim 41, wherein said differentiated tissue is the backbone.
- 49. The morphant of claim 41, wherein said differentiated tissue is the head.
- 50. The morphant of claim 41, wherein said differentiated tissue is a limb.
- 51. The morphant of claim 41, wherein said differentiated tissue is a pigment cell.
- 52. A teleost morphant, wherein the morphant phenotype of said teleost morphant corresponds to a phenotype characteristic of a disease condition.

53. The morphant of claim 52, wherein said disease condition is selected from the group consisting of porphyria and cyclopia.
54. A method of identifying a nucleic acid associated with a disease condition, said method comprising:
- a) generating a teleost morphant having a morphant phenotype that corresponds to said phenotype characteristic of said disease condition, and
 - b) identifying the nucleic acid target of the morpholino-modified polynucleotide in said teleost morphant, wherein said nucleic acid target of said morpholino-modified polynucleotide is the nucleic acid associated with said disease condition.
55. A method for assessing the effect of a drug on a morphant, said method comprising:
- a) contacting said morphant with said drug, and
 - b) assessing the phenotype of said morphant subsequent to contact with said drug.
56. The method of claim 55, wherein said phenotype of said morphant is not altered subsequent to contact with said drug.
57. The method of claim 55, wherein said phenotype of said morphant is replaced by a less severe phenotype subsequent to contact with said drug.
58. The method of claim 55, wherein said phenotype of said morphant, subsequent to contact with said drug, is correlated with a change in the activity of a biomarker.
59. A method of reducing expression from a selected nucleic acid in an animal, said method comprising contacting said animal with at least two polynucleotide analogues that are complementary to different regions of said selected nucleic acid, and wherein said at least two polynucleotide analogues are more effective in reducing expression from said selected nucleic acid than either of said at least two polynucleotide analogues alone.
60. The method of claim 59, wherein said at least two polynucleotide analogues act synergistically to reduce expression from said selected nucleic acid.
61. The method of claim 60, wherein said at least two polynucleotide analogues reduce expression from said selected nucleic acid by a synergy factor of 3.

62. The method of claim 60, wherein said at least two polynucleotide analogues reduce expression from said selected nucleic acid by a synergy factor of 5.
63. The method of claim 60, wherein said at least two polynucleotide analogues reduce expression from said selected nucleic acid by a synergy factor of 10.
64. The method of claim 59, wherein said at least two polynucleotide analogues are morpholino-modified polynucleotides.
65. A composition comprising at least two different morpholino-modified polynucleotides and a pharmaceutically acceptable carrier, wherein said at least two morpholino-modified polynucleotides target the same selected nucleic acid.
66. The composition of claim 65, wherein said at least two different morpholino-modified polynucleotides are complementary to non-overlapping regions of said selected nucleic acid.
67. The composition of claim 66, wherein said non-overlapping regions are separated by more than 1 000 nucleotides.